Impact of Rolandic Epilepsy on Language, Cognitive, and Behavioral Functioning in Children

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Impact of Rolandic Epilepsy on Language, Cognitive, and Behavioral Functioning in Children: A Review

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Abstract

Aim The objective of this narrative review was to investigate how the clinical aspects, such as age-at-onset, epilepsy duration, centrotemporal spikes, spike location, and seizure frequency, affect various domains of language, cognition, and behavior in children with benign childhood epilepsy.

Method Data were collected using various research databases, including Wiley Online Library, PubMed Central, Elsevier ClinicalKey, and Springer Complete Journals. Keywords such as "Benign Childhood Epilepsy" or "BECTS and language impairment" were used among other terms. Case reports, meta-analyses, and reviews were excluded.

Results Children with benign childhood epilepsy are mainly impaired in semantic processing (receptive language), working memory, attention/inhibitory control, complex visuospatial skills, and social skills. Functional magnetic resonance imaging reveals not only structural abnormalities, but also alterations in language, sensorimotor, attentional, and social networks, suggesting long-term consequences.

Conclusion It so seems that the occurrence of centrotemporal spikes (with or without seizures), especially at a young age (below 6 years) and for an extended period of time, is the most meaningful contributor to the language, cognitive, and behavioral deficits in benign childhood epilepsy with centrotemporal spikes (BECTS), while the distribution of centrotemporal spikes (left, right, bilateral) seems of only little significance.

Keywords
- BECTS
- neuropsychological
- children

Introduction

Benign childhood epilepsy with centrotemporal spikes (BECTS) is the most common form of epilepsy among epilepsies of childhood which generally occurs between 3 and 13 years of age and spontaneously resolves by adolescence. A typical electroencephalogram (EEG) in an individual with BECTS would show unilateral or bilateral spike wave discharges in the central and temporal regions, mostly during sleep. BECTS is known for its benign nature with low seizure frequency and spontaneous remission.[1]

However, in the course of over 40 years of research, general consensus has been reached that benign childhood epilepsy should no longer be considered "benign" for a multitude of deficits have been found in the language,[2–30] cognitive,[4,5,9–11 18,19,21,22,26,30–53] and behavioral abilities[22,35,36,50,54–60] of affected children with sometimes lasting effects, particularly in verbal domains.[18,25,27,39] In addition to that, intelligence quotient (IQ) is sometimes below the normal range, contrary to what was originally thought.[5,17,22,24–28,31,34,44,48–50,61–67] Recent improvements in neuroimaging techniques have illustrated alterations in the language,[65,68–70,72,74,75,78,79,81–84] language and sensorimotor,[71,73,76,77,80Q3] attentional,[85] and social networks[86] in the epileptic brain, as well as structural abnormalities,[63,76,87–99] suggesting that BECTS affects these functions in the long term. Since centrotemporal spikes (CTS;

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with or without accompanying seizures) occur at a time when children's brains are still in the development phase, the scientific community now generally accepts that normal brain maturation may be disturbed.

Despite the much-researched epilepsy disorder, the impact of certain epilepsy-related factors, such as age-at-onset and duration since epilepsy onset, the effects of CTS dependent on its location (left, right, bilateral), as well as seizure frequency, remain rather unknown. Over the years, conflicting results have emerged from studies that have looked into these variables. Therefore, this narrative review is written with the intent to shed new light on these controversies. More specifically, this study attempts to investigate the influence of the epileptic syndrome as characterized by age-at-onset, epilepsy duration, CTS, spike location, and seizure frequency on the language, cognitive, and behavioral abilities in children, because a better understanding of the disease would aid in the development of new and improved intervention plans.

What lies beyond the scope of the study, however, is the discussion concerning the impact of antiepileptic drugs (AEDs). While research has shown that AEDs could reduce the number of spikes, a debate has ensued as to whether these drugs ameliorate neuropsychological functions or rather deteriorate these further. If one is interested, please consult refs. 43 and102–107 or see Lagae[108] for a review on potential side effects. Also, not incorporated are genetic factors, for this study centers around the consequences of epilepsy rather than its causes.

This article is structured as follows: the first section of the body deals with intelligence testing in BECTS, followed by two sections on language functioning, starting with specific academic skills. Next, cognitive issues are addressed on topics of executive and memory functioning, as well as visuospatial skills. Lastly, insights into behavioral functioning are given. The "Results" section concludes with some recent neuroimaging findings.

Methods

Studies were collected using various research databases such as Wiley Online Library, Elsevier ClinicalKey, Directory of Open Access Journals, Karger UKB, PubMed Central, Wiley-Blackwell Backfiles, Ingenta Open Access Content, Cambridge Journals, Academic Search Premier, SAGE Premier, and Springer Complete Journals. Keywords and phrases along the lines of "benign childhood epilepsy with centro-temporal spikes," "BECTS and language impairment," "cognitive deficits in BECTS," and "neuropsychological assessment in BECTS" were used. Articles in any language other than English were not consulted. Also excluded from data collection and/or analysis were case reports, meta-analyses, reviews, and studies with less than 10 participants. The final inclusion of publications totaled 130 of which 51 studies between 1975 and 2018 were elucidated in detail.

Results

Intelligence Testing

Contrary to what is generally believed, children with BECTS do not always possess intelligence within the normal range. This study looked into 82 studies that tested intelligence. The results are presented in ►**Table 1**. In total, 32 studies (39%) found individuals with extremely low or extremely high intelligence profiles. Moreover, 15 studies (18.3%) found significantly lower IQ scores in BECTS children when they were compared with neurotypical controls. This indicates that nonnormal intelligence is quite common for children with childhood epilepsy. Yet, 35 studies (42.7%) have excluded children with an IQ below 85. Another issue to be addressed is that of assessment type. Full-Scale IQ has only been conducted in 57 studies (69.5%). Another 16 studies (19.5%) focused solely on either verbal or nonverbal IQ. From the remaining 9 studies (10.10%), it is not exactly clear what kind of intelligence testing has been done. While the majority of studies (64.6%) reported the IQ mean, only

Table 1 Intelligence assessment in BECTS

Intelligence assessment in 82 studies		Total number (%) of studies	
		Number (%)	Studies
Category			
Nonnormal IQ	IQ $<$ 85	17 (20.7)	24,27,31,44,48–50,62,65–67,88,98,100,101,112,118
	IQ $\geq$ 115	15 (18.3)	17,20,23,24,31,44,48–50,65,88,100,101,112,118
	IQ BECTS sign $<$ controls	15 (18.3)	2,6,21,34,48,58,61,73,89,93,95,98,114,124,125
Exclusion of children	IQ $<$ 85	35 (42.7)	4,6–9,11–13,15,17,21,23,41,42,47,51,52,54,58,68,72,73,80,93–95,100 101,107,109–114
Assessment type	Full-Scale IQ	57 (69.5)	8,9,13–16,21–24,28,31,34,42,44,45,47–49,51,52,54,58,62,64–68,70–75,78 85,87–89,91–93,95,100,101,105,109–111,114–116,118,123–125
	Verbal IQ-only	2 (2.4)	6,20
	Performance IQ-only	14 (17.1)	2–5,10,17,25,27,38,50,61,82,113,117
Aspect of IQ reported	IQ mean	53 (64.6)	2,4–6,13,15–17,20–22,24,34,38,42,44,48,50–52,54,58,61,62,65,66,70,71,73 74,78,82,85,87–89,91–93,95,98,100,101,105,109–111,114–116,118,124,125
	IQ range	19 (23.2)	14,17,20,23,24,31,44,48–50,58,62,64,65,88,100,101 112,118

Abbreviations: BECTS, benign childhood epilepsy with centrotemporal spikes; IQ, intelligence quotient.

19 studies (23.2%) reported the IQ range. It is essential, however, to always note down the IQ range.

Academic Achievement

Research into academic skills has been widely undertaken. A considerable number of studies documented specific learning disabilities and general shortcomings in reading, spelling, writing, arithmetic, or phonological awareness skills in BECTS (►**Table 2**).

Overvliet et al[15] investigated the number of BECTS children who had duplicated a year in school or had taken speech therapy in the past and concluded that early language impairments could be a precursor to the diagnosis of epilepsy. Other authors reported that these children repeat

Table 2 Academic skills in benign childhood epilepsy with centrotemporal spikes

Neuropsychological outcomes			Main contributions	
			Deficits found in	Epilepsy effect for
Topics				
Academic skills	Currie et al[2]	*N* = 25 (6–12 y)	Word reading Reading comprehension Nonverbal reasoning	–
	Filippini et al[4]	*N* = 15 (5–13 y)	(Non)word reading Phonological skills	–
	Miziara et al[11]	*N* = 40 (7–13 y)	Reading Writing Arithmetic Auditory processing	–
	Ebus et al[13]	*N* = 26 (6–12 y)	Reading Verbal IQ	EA
	Monjauze et al[25]	*N* = 16 (6–15 y)	Reading Spelling Morphosyntax	CTS location Epilepsy duration
Phonological awareness Working memory	Leôncio et al[5]	*N* = 21 (6–13 y)	Phonological Awareness Working Memory	–
	Northcott et al[26]	*N* = 42 (6–12 y)	Basic reading Nonword reading Nonword spelling Memory Phonological skills	–
Learning disabilities	Oliveira et al[8]	*N* = 31 (7–14 y)	Reading Writing Memory Arithmetic Phonological skills	–
	Filippini et al[10]	*N* = 33 (4–12 y)	Phonological WM Learning (reading, writing, arithmetic)	EA Early onset
	Piccinelli et al[19]	*N* = 20 (7–12 y)	Reading Writing Calculation Sustained attention	EA Early onset
	Canavese et al[23]	*N* = 10 (9–11 y)	Calculation	–
	Papavasiliou et al[27]	*N* = 32 (7–16 y)	Spelling Reading comprehension	Seizure frequency Epilepsy duration
Academic delay	Overvliet et al[9]	*N* = 25 (8–14 y)	CELF-4: Word Definitions Sentence Repetition Word Category Understanding Spoken Paragraphs	–
	Pinton et al[24]	*N* = 18 (4–8 y)	Reading Spelling Numeracy Visual memory Visual attention Selective attention	

Abbreviations: CELF-4, Clinical Evaluation of Language Fundamentals-Fourth Edition; CTS, centrotemporal spikes; EA, epileptic activity; IQ, intelligence quotient; WM, working memory.

classes more often than their neurotypical peers,[9,14,24,25] which could result in academic delay.

Some authors proposed that weaknesses in the phonological loop and visuospatial sketchpad contribute to reading and spelling difficulties.[4,5] If true, it would be in line with the hypothesis that learning disabilities are phonological in nature.[119] Filippini et al[4] explained that the spoonerisms they used were particularly difficult for the experimental group considering that this task is complex and demanding with regards phonological working memory (WM), leading to WM capacity dysfunction. Other studies have documented phonological deficiencies in BECTS.[7,8,14,22]

Only few studies have found an effect for epilepsy variables. For example, Piccinelli et al[19] found that $\geq$ 50% of epileptiform activity (EA) on sleep EEG strongly correlated with specific learning disabilities, especially in combination with early onset ($<$ 8 years). Similarly, Filippini et al[10] demonstrated that the occurrence of spikes during $\geq$ 85% of nonrapid eye movement sleep showed language deficits in the clinical range in children with atypical epilepsy. Problems were less severe in children with a lower spike index (SI). It was also reported that those with early onset (around 8 years of age) were at a higher risk for developing neuropsychological problems. Another example is a study conducted by Ebus et al[13] who found a connection between verbal IQ, reading performances, and the amount of nocturnal EA in a cohort of 26 children with BECTS. Similarly, Monjauze et al[25] reported that children with a unilateral, right-sided focus, and longer duration of epilepsy had the worst outcomes in reading, spelling, and morphosyntax. Papavasiliou et al[27] discovered that severe written language problems were more presented in children with higher seizure frequency and longer epilepsy duration. By contrast, the results obtained by Canavese et al[23] and Northcott et al[22,26] only revealed minimal associations.

To conclude, in comparison to typically developing peers, BECTS children seem to experience academic problems early in school. This indicates that the comorbidity between BECTS and specific learning disabilities (e.g., dyslexia) may be higher than expected. EA mainly occurs during sleep, making the exact age at which epilepsy occurs difficult to determine. This explains why learning problems may predate a diagnosis of epilepsy. For BECTS to be detected sooner, early EEG testing would have to be in order.

Language Functioning

Outside of scholastic difficulties, receptive and expressive elements of language are compromised in different ways in BECTS (►**Table 3**).

Jurkevičienė et al[12] found a clear relationship between early onset and language outcome in a large cohort of 61 children with BECTS. Verbal dysfunction was most severe in children younger than 6 years. According to the authors, intermittent interruptions of spike-wave discharges may disturb the process of functional cortical reorganization, making it difficult for noninjured hemispheres or otherwise noninjured regions to overtake and develop a new function. Similarly, studying 63 children with epilepsy of childhood, Ma et al[6] corroborated that children below 6 years were more

Table 3 Language skills in BECTS

Neuropsychological outcomes			Main contributions	
			Deficits found in	Epilepsy effect for
Topics				
Lexical processing Semantic processing	Verly et al[3]	N = 15 (7–14 y)	CELF: Concepts and Following Directions Formulating Sentences Word Associations Number Repetition Forward	–
	Ma et al[6]	N = 63 (8–11 y)	Verbal comprehension Word reasoning Vocabulary	Early onset
	Jurkevičienė et al[12]	N = 61 (7–13 y)	Verbal fluency Lexical comprehension	Early onset
	Riva et al[21]	N = 24 (7–12 y)	Phonemic fluency Lexical comprehension	EA CTS location
Phonological processing Auditory processing Speech	Bedoin et al[14]	N = 18 (7–11 y)	Phonological processing	EA Early onset CTS location
	Danielsson and Petermann[17]	N = 25 (4–7 y)	Speech	–
	Boatman et al[20]	N = 7 (7–11 y)	Speech Auditory processing	EA
	Lundberg et al[29]	N = 20 (8–14 y)	Speech Auditory processing	–

Abbreviations: BECTS, benign childhood epilepsy with centrotemporal spikes; CELF, Clinical Evaluation of Language Fundamentals; CTS, centrotemporal spikes; EA, epileptic activity.

gravely impaired vis-à-vis older children. The authors support the idea that nocturnal CTS may interfere with the process of functional reorganization of language networks. Likewise, Bedoin et al[14] suggested that EA at an early age could have disturbing effects on the maturational process of phonological processing, which is crucial for receptive language.

A relation between diurnal spiking and auditory impairment was identified by Boatman et al.[20] They evaluated cortical auditory function, including speech recognition in seven BECTS patients. Results revealed a dysfunction of the nonprimary auditory cortex. The patients with worst performances showed CTS on awake EEG. Speech-related problems were also found in works by Lundberg et al[29] and Danielsson and Petermann.[17] Another study pointed out the detrimental effects of $>$ 10% of spikes on awake EEG on cognitive performances in epileptic children, regardless of syndrome type or other EEG-related traits.[101]

Riva et al[21] studied 24 children with an active focus. They were submitted to several language tests designed to measure phonemic fluency, verbal recall of semantic knowledge, and lexical comprehension. Results revealed that these children had mild language deficits. It was also demonstrated that multifocal spikes, a temporal focus (as opposed to nontemporal), and a high SI during wakefulness impacted on some of the language tasks. The authors pointed out that the EEG was not obtained until approximately 2 months prior to assessment and that therefore the results ought to be interpreted with caution since BECTS is a changeable condition, especially in terms of the rate and localization of spikes.

On the whole, children with BECTS are impaired in several language domains beyond reading and spelling. Receptive language (lexical, semantic, or auditory) seems to be the weakest link. The evidence points to early onset but also the occurrence of EA to seriously impinge on aspects of language functioning, especially when this happens during a sensitive period for language development in childhood. It is important to remember, however, that epilepsy has certain traits that may vary from moment to moment in the same individual. Therefore, it would be best to keep the time window between EEG recordings and behavioral assessment as narrow as possible.

Executive Functioning

The most documented cognitive problem in BECTS is that of executive function (EF). This is an umbrella term for cognitive processes associated with organizing behavior (e.g., planning, inhibition, mental flexibility, WM). These constructs are difficult to separate from other modalities, such as attention, memory, and processing speed.[37] As discussed before, a deficit in phonological WM was demonstrated by Filippini et al.[4] One of the tasks used was a word span task, which requires the manipulation of information stored in WM by comparing the recall of words in both serial and alphabetical order.

Digit span strings are the most documented measures of WM in the BECTS literature with regard to the central executive and phonological loop. One appeal that these tasks have is sensitivity to long-term dysfunction. While deficits in digit span (forward and/or backward) have been widely reported,[5,10,11,21,33,40,43,48,49] these deficits have not always been confirmed.[4,9,18,19,26,32,35,39,44,50,52]

Cerminara et al[41] used the multicomponent model of attentional function and found significant impairments in several domains of attention in 21 children aged 7 to 14 years with epilepsy. While they tried linking disease onset to neuropsychological outcomes, they could not find a link. This is in contrast with the results of Deltour et al[44] who documented that a limitation of attentional capacity, irrespective of modality, is in fact associated with earlier onset of seizures and longer duration of active epilepsy. They suggested that these factors play a role in attentional deficits given that the prefrontal areas and surrounding areas associated with functions of attention and control have not yet matured at the time epilepsy occurs. Therefore, these factors might interfere with the development of those areas.

Chevalier et al[53] assessed impulse control in 13 children aged 6 to 12 years with the intent to evaluate possible consequences of BECTS on frontal lobe functions. Results revealed significantly more errors in several tasks compared with 13 controls. This illustrates that BECTS children are somewhat impaired in response inhibition, which may point to relatively poor functioning of the frontal lobes.

Neri et al[39] aimed to verify the influence of age-at-onset on measures of EF in 25 children aged 6 to 15 years with childhood epilepsy. Most children were no longer in the active phase of their disease. These children, however, still showed impairments. It was found that children with later onset (after 5.7 years) had better scores on semantic fluency than those with early onset (before 5.7 years). The authors suggested that early onset of seizures could hinder brain development in that the volumes of white matter slowly become reduced, leading to a reduction of cortical connectivity. However, a study that looked into white matter volume could not find any correlations between the language performances and cortical thinning, despite that cortical abnormalities were in fact found in children with epilepsy who were still in a critical phase of brain development.[97]

Taken together, the findings seem to indicate that underdevelopment of the frontal lobes could result in attentional and executive deficits. The children who acquire epilepsy at an early stage in life appear to be the most vulnerable. On that note, early assessments are necessary to establish, plan, and execute early school interventions so that the negative impact of childhood epilepsy on functions of cognition can be somewhat abated.

Memory Functioning

Memory and learning is another domain in BECTS that is of concern. Considering that this domain merges with verbal and EFs, pure data are scarce.

Most recently, Chan et al[34] studied sleep-to-memory consolidation in 22 children aged 6 to 12 years with childhood epilepsy and 21 healthy subjects. Memory assessment consisted of a verbal and visual-spatial task. Their findings suggested that sleep-related consolidation is intact in

childhood epilepsy. It may even serve as a compensatory mechanism to maintain cognitive function. A longer history of epilepsy only partially correlated with test results. The authors indicated that children could aid learning by recapitulating important facts they have learned throughout the day before bedtime.

In a comparison study with frontal lobe epilepsy), childhood absence epilepsy, and BECTS, Lopes et al[37] examined memory in 90 children (30 children per group between the ages of 6 and 15 years). The measures used were designed to test verbal and visual (working) memory. It was found that children with BECTS particularly struggled with word recognition. In this study, disease onset only minimally influenced the results.

Vintan et al[38] assessed various aspects of visual-spatial memory and learning in 18 untreated BECTS children aged 6 to 14 years and 18 age-matched controls. They found impairments in pattern and spatial recognition memory in the epilepsy group, as well as correlations between SI and several tests. Visual memory (and the recognition of newly learned visual information) is a highly complex function, because activities of the frontoparietal and visual cortical neurons constantly interact with newly formed functional connections (as opposed to operating on their own).[120]

Vago et al[42] assessed verbal learning and retrieval, including the implementation of learning strategies in 24 BECTS children aged 7 to 12 years and 16 controls. In comparison with a healthy group, children younger than 10 years had not only significant learning difficulties, but were also less efficient in adopting a new strategy, unlike subjects above 10 years. A contributing factor might be that the younger group presented with multifocal spikes.

Metz-Lutz and Filippini[45] studied children with typical and atypical epilepsy. Children were labeled "typical" when the focal spike wave discharges occurred against a normal EEG and "atypical" when the early EEG displayed a slow spike wave focus or asynchronous foci. The latter group had significantly lower intelligence scores, along with lower verbal short-term memory and verbal learning scores. With the exception of verbal short-term memory in the atypical group, results improved significantly upon remission. Another study that examined children beyond the active phase of epilepsy was the one conducted by Lindgren et al.[117] They followed 26 children aged 7 to 15 years in the course of 3 years. Deficits in memory, verbal fluency, and learning of auditory-verbal memory were initially found, whereas new learning for visual-spatial material seemed to be unaffected. But at the second assessment, no significant differences were found between the experimental and control groups in the ability for memory and learning of both auditory-verbal and visual-spatial material, except for verbal fluency.

In summary, short memory for visual or verbal material is ostensibly compromised in children with BECTS. More studies are needed to determine if previous memory impairments truly subside upon remission. But while children are still in the active phase, intervention plans should be aimed toward memory enhancement, given that memory encompasses many facets of everyday life. So saying, future studies ought to include measures of everyday memory as traditional memory tests may not capture all the memory abilities of children with epilepsy.

Visuospatial Skills

This is a domain somewhat neglected in the BECTS literature. There are no recent studies on this topic. However, the available data are still relevant to this study. In a combined magnetoencephalography/EEG study, Wolff et al[30] determined the location of spikes by dipole source estimation in a cohort of 27 children. Three main locations were identified: left perisylvian, right perisylvian, and occipital locations. The majority of children had spikes in the left perisylvian regions. They had the worst language scores, although global intelligence was unaffected. Children with occipital spikes had significantly lower scores in complex visual transformation tasks, in contrast to global IQ, language processing, and pattern recognition tasks. High-level cognitive functions seemed to be most susceptible to the influence of the discharges, as they rely upon the interaction processes between various cortical areas, meaning that cortical activations in the visuospatial system increase with the level of task demand.[121]

Völkl-Kernstock et al[47] investigated spatial performance in 22 patients and 22 controls aged 6 to 10 years using tests from the Kaufman Assessment Battery for Children and Differential Neuropsychological Test. These assess complex spatial perception, orientation, and memory. Specifically, these tests demand from children to reproduce different spatial arrangements and accurately estimate the angles, distances, and positions of geometric figures. Participants were significantly impaired in complex spatial memory and perception, although basic spatial perception was intact. When reviewing all the EEG recordings over time, not one child had a stable focus in one hemisphere, supporting the notion that focus location is ever-changeable.

Bedoin et al[46] distinguished between 6 children with a left-sided focus and 6 children with a right-sided focus and compared their performances in a verbal and visuospatial/attentional task to that of 12 control children. It was demonstrated that the children with a right-sided focus underperformed in the visuospatial task relative to those with a left-sided focus. Additionally, the so-called left-hemisphere advantage for verbal tasks was not observed in those with a left-sided focus, meaning that the representation of language functions is atypically bilateral in patients with childhood epilepsy. Patients showed strong impulsivity and distractibility throughout assessment, despite that those with scholastic or behavioral problems have been excluded. This suggests impairments in EFs, regardless of the focus side. The authors indicated that the focus side is not a fixed feature, as the epileptic discharges might shift from one hemisphere to the other. A previous study that likewise attempted to link neuropsychological dysfunction to CTS lateralization was performed in 1994 by Piccirilli et al.[51] BECTS children between 9 and 13 years of age and 15 controls were subjected to a more complex version of a

figure cancellation task. This is a test that assesses the processing of visuospatial information, as well as attentional mechanisms. Patients with a left, right, or bilateral focus were divided into separate groups. No meaningful differences were found between those with a left-sided focus and controls, whereas patients with a right-sided focus—and to a larger extent—those with EA in both hemispheres, had worse performances. These results suggest that CTS alone (without seizures) cause enough damage which leads to functional alterations in cognitive processing. Overall, children with childhood epilepsy have deficits in spatial perception, orientation, and memory, which cannot be attributed to intellectual disability. Focus location seems only of relative importance, seeing that discharges could disseminate throughout the brain.

Behavioral Functioning

Back in 1975, Heijbel and Bohman[60] published an article on intelligence, behavior, and school adjustment in children with childhood epilepsy. While the children did not seem to exhibit any behavioral problems, their visuomotor coordination seemed to be impaired. In more recent years, literature has emerged that offers contradictory findings about the matter. Problems ranging from hyperactivity and aggression to anxiety, depression, and social conduct have been documented.[22,35,50,54–58] These findings are oftentimes predicated on questionnaires and interviews with parents and teachers. A high comorbidity seems to exist between children with BECTS and children with attention deficit hyperactivity disorder (ADHD).[36,59]

Most recently, Bektaş et al[54] investigated the relationship between seizure timing and psychosocial and behavioral functioning in 46 children with BECTS. Children with seizures were divided between those who experience seizures shortly after falling asleep and shortly before awakening. The results showed that children who endured seizures shortly after falling asleep exhibited a wide array of emotional problems, including hyperactivity and concentration, emotional distress, and problems on the social front. The results are in agreement with Völkl-Kernstock et al[58] who reported that children with BECTS had more difficulties than their peers with interpersonal relationships. In addition, these children showed disturbing behaviors in the classroom. The Child Behavior Checklist (CBCL) revealed significant problems with attention, aggression, anxiety, and depression.

Kim et al[36] investigated attention impairment in children with epilepsy with ADHD and those without ADHD. After the medical records of the patients were reviewed, along with the mean scores obtained from a behavioral test, it was revealed that 48 out of 74 patients (64.9%) met the criteria for ADHD. The seizure frequency was higher in treated ADHD patients than in those untreated. And patients with a high SI ($\geq$ 40 p/m) or with frequent seizures prior to diagnosis were significantly impaired in visual selective attention.

Eom et al[35] examined the effects of exercise therapy in children with childhood epilepsy. At baseline, children suffered substantial behavioral problems, but after program completion, improvements were observed in mood, depression, and social problems. Children also improved in some attentional and EFs. The authors suggested that these therapies could lead to better self-esteem and social integration, which could enhance their quality of life. Northcott et al[22] actually assessed quality of life with the Quality of Life in Child Epilepsy Questionnaire, and it was revealed that children with childhood epilepsy have a lesser quality of life than those who do not exhibit the syndrome. These differences were most pronounced in domains of self-esteem and general health.

Samaitienė et al[56] studied 43 BECTS children by means of the CBCL. Significant results were found with respect to anxiety and aggression, hyperactivity, and social problems, especially for those on medication and with longer duration of epilepsy. Age at seizure onset was also correlated with more oppositional behavior. Building on these findings, Samaitienė et al[55] followed up on this patient group and discovered that those who had suffered through seizures in the past 6 months were more disturbed in their behaviors.

Sarco et al[57] aimed to investigate whether a relationship exists between the SI and parental ratings of psychosocial adjustment and executive functioning in 21 children with BECTS. It was found that a high SI for both sleep and wakefulness was associated with symptoms of depression, aggression, and conduct problems. In addition, higher SI during sleep was associated with anxiety and executive dysfunction. No correlation was found between hyperactivity and SI. The authors concluded that a higher SI may be predictive of behavioral problems.

In conclusion, the problems children with epilepsy suffer lie beyond that of scholastic and language skills and overall cognition. Since children tend to internalize and withdraw within themselves, their problems are not always apparent. In particular, children with seizures after falling asleep ought to be screened for behavioral problems. Intervention plans should be aimed toward decreasing possible feelings of anger, anxieties, and depression and increasing their quality of life and general health, possibly by enforcing exercise therapy or other forms of group activities.

Neuroimaging Findings

The language, cognitive, and behavioral changes correspond with changes in the structural and functional neuroanatomy in children with BECTS. Such changes or anomalies are particularly visible in language networks,[65,68–70,72,74,75,78,79,81–84] and also in language and sensorimotor,[71,73,76,77,80] attentional,[85] and even social networks.[86] Given the abundance of data, the focus of this paragraph will be on a selection of studies that have been published in 2017 and 2018 only.

Kim et al[68] researched the relationship between cognitive ability and modified functional connectivity (FC) in the resting-state brain networks of 19 BECTS patients (mean age: 13:4 years) and 23 controls (mean age: 12:1 years). Intelligence assessments and tests of memory and EF were conducted. It was found that the study group had a more profound performance IQ > verbal IQ discrepancy in comparison to controls. BECTS patients also showed more enhanced FC to voxels in regions related to the semantic

processing of spoken language. This could be a compensatory mechanism for poor verbal cognition, according to the authors. This is not the first study to have found alterations in FC. Older studies have reported that rolandic epilepsy alters FC between language and motor networks either in the resting-state or during word-generation tasks.[75,77,78,82,85]

Ofer et al[88] aimed to investigate cognitive development (CD) and socioemotional development (SED) in 10 patients aged 7 to 13 years with active BECTS in relation to default mode network (DMN) connectivity and network topology. It was postulated that a more complicated CD/SED in these children might be associated with aberrant organization of the DMN, presumably owing to the involvement of DMN components to spike-generating cortex regions. Intelligence and personality traits were assessed. The researchers found evidence that a more complex cognitive/SED is "mediated by a common pathomechanism related to an aberrant organization and a possibly resulting functional deficit within the DMN." Notably, the children with high seizure frequency and early disease onset and longer duration have an increased risk for specific cognitive deficits and a more complicated SED.

Jiang et al[87] investigated differences in cortical folding and its structural covariance networks between 26 BECTS children (mean age: 10:3 years) and 26 healthy controls (mean age: 11:3 years) to confirm CTS effects on a developing brain. Children with BECTS exhibited abnormal foci of cortical gyrification in bilateral Sylvain's fissures and surrounding areas related to emotion, behavior, and language and EFs, indicating preexistence of overfolding cortical sheets and atypical development of higher association cortices. Anomalies in the Sylvian fissure morphology have earlier been detected in Williams syndrome.[121,122] Disrupted node properties in the structural network and a shift in the hub distribution were also observed. Significantly positive relationships were established between the gyrification index, chronological age, and disease duration. The authors suggested that aberrant cortical folding and its nodal properties of structural wiring could underlie the neuroanatomical basis of childhood epilepsy. Their results are generally in line with existing neuroimaging studies.[72–74,77,93,94,121,123–125]

Ciumas et al[86] investigated neuronal responses to emotional stimuli in 13 children with BECTS and 11 control subjects aged 6 to 12 years using event-related functional magnetic resonance imaging (fMRI). They were asked to discriminate between happy, fearful, scrambled, and neutral faces. Perception of human faces is a complex process that relies on a network amid the occipitotemporal cortex.[128–130] In the fearful condition, BECTS children showed significantly less bilateral activation in the insular cortices and in the dorsal striatum, which is interesting, because recent morphometric studies have found delayed thickening of the insular cortex[63] and striatal hypertrophy[94] in BECTS, indicating aberrant maturation of these structures. In the happy condition, children with epilepsy had slower response time opposite to controls. Overall, these findings suggest alterations in the social cognition network and function, especially for identifying fearful faces. In children with temporal lobe epilepsy, it was already observed that emotional recognition is significantly impaired. This dysfunction was most apparent in children with early onset.[126]

Taken together, these findings illustrate that functional and structural neuroanatomical changes take place in the epileptic brain. However, fMRI techniques are restricted to show what the brain looks like *after* epilepsy onset and not before. Therefore, the developmental course of these changes remains unclear. Nevertheless, the abnormalities in various brain networks, even beyond central/temporal regions, are evident, and they support the problems observed through behavioral studies to a large extent (►**Table 4**).

Conclusion

The purpose of this study was to examine the influence of the epileptic syndrome as characterized by disease onset, epilepsy duration, SI, spike location, and seizure frequency on the language, cognitive, and behavioral abilities in children. Before revealing the outcome of this study, some statistics first: only 42 studies (77.7%) of the 54 described have correlated for one or more clinical variables. Of these, 10/20 studies (50%) found an effect for age-at-onset; 8/13 (61.5%) for epilepsy duration; 12/19 (63.1%) for SI, 6/13 (46.1%) for spike distribution; and 4/4 (100%) for seizure frequency. (Due to seizure infrequency, examining this feature is not always possible.) These inconsistencies could be due to small sample size, the use of different assessment tools (individual vs. comprehensive tests), different inclusion criteria (e.g., incorporating children in special education and/or with comorbid disorders), and group heterogeneity (e.g., AED takers and non-AED takers). In any case, the imbalance in the amount of available data makes it challenging to arrive at a fair conclusion. So a bit tentatively the following conclusion can be drawn.

The variables age-at-onset, epilepsy duration, and SI are interrelated. If BECTS occurs at an early age and lasts for a long period of time, brain development is likely to become affected by it, even without accompanying seizures. But whether the SI is high or low does not seem to matter, for children with a low SI have shown impairments in the measures in which they were tested.[23,102] In addition, EEG recordings of spike activity and localization and behavioral testing should always be conducted simultaneously. As CTS tend to shift from side to side,[1] it is pointless to assess EEG traits separately. In point of fact, at least two studies[47,70] failed to properly divide their patient groups according to spike distribution due to focus imbalance. It has been demonstrated, though, that children with bilateral spikes are more severely impaired in their functions than those with unilateral spikes.[22,26]

Generally, the language-related areas as well as functions subserved by the frontal lobes (e.g., EFs) are particularly affected. Children with childhood epilepsy do not only experience language problems, but also attentional problems and social problems. To a smaller extent, they also experience difficulties with complex aspects of memory and visuospatial information. On the whole, children with BECTS suffer through a great deal of challenges in the course of their

Table 4 Neuroimaging findings in BECTS

Neuroimaging studies and their outcomes			Main contributions	
			Alterations found in	Epilepsy effect for
Topics/ROIs				
Functional connectivity (FC) in rolandic and language-related areas	Kim et al[68]	fMRI	Left inferior temporal gyrus (more enhanced FC to voxels) Rolandic/language FC to the left temporal gyrus (correlated negatively with WISC-III)	–
Cognitive development (CD) and socioemotional development (SED) in relation to DMN connectivity and network topology	Ofer et al[88]	fMRI graph theory	Parietal network nodes and midline structures in terms of efficiency and centrality (link found between centrality of the left inferior parietal lobe [IPL] and CD)	Age-at-onset Disease duration Seizure frequency
Cortical gyrification and structural covariance networks	Jiang et al[87]	MRI graph theory	Bilateral Sylvain fissures and the left pars triangularis, temporal, rostral middle frontal, lateral orbitofrontal, and supramarginal areas (increased gyrification)	Disease duration
Emotion recognition ROIs: Occipitotemporal cortex, the center of the fusiform gyrus—fusiform face area (FFA), occipital face area (OFA), and superior temporal sulcus (STS)	Ciumas et al[86]	fMRI	Insular cortex, caudate, and lentiform nuclei (reduced bilateral activation)	–

Abbreviations: BECTS, benign childhood epilepsy with centrotemporal spikes; DMN, default mode network; fMRI, functional magnetic resonance imaging; ROI, region of interest; WISC-III, Wechsler Intelligence Scale for Children-III.

disease and even beyond that, for verbal deficiencies do not always resolve after remission. More longitudinal studies are needed to determine if other problems persist beyond the active phase.

Based on these conclusions, this review closes with a few suggestions:

1. Control variables: to examine how childhood epilepsy impacts on various functions, clinical variables (e.g., disease onset) should always be controlled for and authors ought to report about them, even when they do not find an effect.
2. Early EEG assessment: the high comorbidity between BECTS and developmental disorders warrants early EEG testing, so that intervention can begin early.
3. Comprehensive testing: individual measures of language and cognitive function do not always capture the problems BECTS children have in these domains; therefore, a comprehensive test battery should always be used.
4. Matching criteria: since the epileptic syndrome impacts on neuropsychological functions, it is likely that it impacts on intelligence as well. So it is highly recommended to the scientific community not to create a selection bias anymore toward those who have less-than-normal intelligence but to incorporate those with low intelligence profiles.
5. Clinical implications: studies by Chan et al[34] and Eom et al[35] are truly inspiring for their originality and promising results. They should be used to design exercise programs and memory-enhancing strategies so that children with epilepsy could benefit from that in clinical practice.

Conflict of Interest
None declared.

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